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(57) Abstract

Treatment of obesity, especially in man. In the invention an overweight patient is given a daily diet in which t amount of proteinaceous material is restricted below the patient's normal average daily intake of protein, together with daily dose of at least about 0.5 grams of L-tryptophan as appetite-suppressant. Thus, the invention provides a composition for use in the treatment of obesity. That composition comprises L-tryptophan and a protein-restricted diet composition carrier, the amount of L-tryptophan in the composition being such as to provide at least about 0.5 grams of L-tryptoph per daily amount of diet. Preferably, the carrier is a protein-restricted formula diet, the diet comprising on a daily amou basis less than about 100 grams of proteinaceaous material and an energy level of no more than about 1000 Kcals.

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A COMPOSITION AND PACK FOR USE IN THE TREATMENT OF OBESITY

The present invention relates to the treatment of obesity and, in particular, to an agent for the control of appetite, when used together with a low protein diet and compositions containing the same.

The compound L-tryptophan is known as an essential aminoacid and, as such, is known as a compound required for human nutrition. Thus, L-tryptophan is sold in the U.K. in tablet or capsule form for use as a nutritional supplement. Also, L-tryptophan is presently marketed in the U.K. either alone or in combination with pyridoxine hydrochloride (vitamin B6) and ascorbic acid as an agent for the treatment of disorders of the central nervous system, in particular as an anti-depressant, a sleep-inducer and/or a mood calmer.

Furthermore, various investigators have looked at the use of L-tryptophan in the control of appetite in human beings, but generally speaking either have obtained ambiguous results or results which show that control of appetite is not obtained. Thus, Weinberger et al in Life Sciences, Vol. 22, pages 1595 to 1602, in an article entitled "Failure of tryptophan load-induced increases in brain serotonin to alter food intake in the rat" report that:

> "The effects on food consumption of 50 and 100 mg/kg l-tryptophan injections, versus control saline treatment, were compared in 24-hour food-deprived rats at two time points in the rats' daily light-dark cycle. No effect of the two tryptophan doses, relative to the saline treatment, on food intake was observed, although

tryptophan loading significantly raised brain tryptophan, serotonin, and 5-hydroxyindoleacetic acid levels, in a dose-dependent manner, over baseline concentrations."

Furthermore, Wurtman et al in International Journal of Eating Disorders, 1981, Vol. 1, pages 2 to 15, in an article entitled "Carbohydrate craving in obese people: suppression by treatments affecting serotoninergic transmission" report that:

"Tryptophan significantly diminished carbohydrate intake in three of the eight treated subjects, and increased it in one subject; it did not significantly modify snacking patterns in the group as a whole."

And that:

"Tryptophan has not been reported to have consistent effects on hunger per se, and thus probably did not exert its effect by simply suppressing appetite among the three responders. Weinberger et al ..... [supra] ....found no reduction in food intake among food-deprived rats during the two hours after treatment with sufficient tryptophan (50 or 100 mg/kg) to raise brain tryptophan levels. Latham and Blundell (1979) observed a slight decrease in food intake among rats feeding freely on a single test diet, and no change in total daily food intake among food-deprived animals. The decrease in food intake resulted from a decrease in meal size and an increase in the between-meal interval."

In addition, Gibbons et al in Pharmacol. Biochem. Behav., 1981, August, 15(2), pages 201 to 206, in an article entitled "L-tryptophan's effects on mouse killing, feeding, drinking, locomotion, and brain serotonin" report that:

"Tests in 24 hour food deprived rats revealed that

feeding behavior was also significantly decreased about 30% by tryptophan injections (50-100 mg/kg IP)."

Also, Rogers et al in International Journal of Obesity, 1979, Vol. 3, page 94, in an article entitled "Effect of tryptophan and anorectic drugs on food intake, hunger, food selection and microstructure of eating in man" report that:

"In Expt. I oral administration of 2 g or 4 g of tryptophan produced no clear effect upon the total amount of food consumed or upon the selection of protein or carbohydrate provided in a simple test meal."

Moreover in a recent review entitled "Serotonin and Appetite" in Neuropharmacology, Vol. 23, No. 12B, 1984, at pages 1537 to 1551, J.E. Blundell reports that:

"The effect of tryptophan on food intake is not massive (at the moderate dose normally administered) and any disturbance or contamination during collection of data could easily mask the anorexic action. Significantly, when the effects of tryptophan were monitored continuously in a controlled laboratory environment, a clear effect was demonstrated on free-feeding rats which lasted for 4 hours after administration. This effect was characterised by a reduction in meal size. Moreover, in deprived rats, tryptophan reduced the magnitude of the first enormous meal normally consumed by rats when allowed access to food (Latham and Blundell, 1979)."

Accordingly, while in the above prior art there are suggestions that tryptophan may have some small effect on food intake, there is nothing in that prior art to suggest either that tryptophan can have a pronounced effect on food intake and/or as to the manner in which the effect of tryptophan can be made

consistent.

Furthermore, in U.S. Specification No. 4,210,637 Wurtman et al suggest that a composition for suppressing appetite for calories as carbohydrates may be based on tryptophan. Such a composition is broadly defined as one which, when administered to an animal (prior to consuming food), decreases appetite for calories as carbohydrates which consists essentially of an amount of tryptophan effective to increase brain serotonin levels and a carbohydrate in an amount effective to cause insulin to be released in the animal.

In that earlier invention, generally the weight ratio of the tryptophan to the carbohydrate(s) is between about 0.05 and about 5.0, more usually between about 0.20 and about 2.0. The compositions of that invention are administered in an amount sufficient to effect increase in brain serotonin levels while not being administered in such large amounts as seriously to reduce the brain levels of other neurotransmitters needed for normal functioning such as dopamine, norepinephrine, acetylcholine, or the non-essential amino acids. Generally also, the compositions of that invention are administered in an amount of between about 10 mg/kg and about 100 mg/kg of tryptophan, and 10 mg/kg and 300 mg/kg of carbohydrate, more usually between 20 mg/kg and about 50 mg/kg of tryptophan, and 30 mg/kg and 150 mg/kg of carbohydrate. Typical unit dosage forms useful for oral administration are said to range between about 0.5 grams and about 15 grams, and more usually between about 1 gram and about 10 grams.

Thus, the earlier invention provides a method and composition for suppressing appetite for calories (as carbohydrates) **while elevating the percent of total calories that is consumed as protein.** The invention is based upon the discovery that a combination of tryptophan and a carbohydrate (which causes insulin

secretion) selectively suppresses the appetite for calories (as carbohydrates). The mixture of tryptophan and said carbohydrate can be administered alone, in admixture with one or more amino acids normally found in the blood plasma, or with caffeine or another mild stimulant, to override the mixture's natural sedating effects. It is said to be believed that the compositions function by mechanisms which involve the enhancement of brain serotonin synthesis, serotonin being a neurotransmitter involved in the control of appetite.

However, I have now found surprisingly that L-tryptophan can be used as a powerful agent in the control of appetite provided it is administered in conjunction with an essentially nutritionally complete diet which has a content of protein, typically as calculated on a daily basis, below that normally taken by the subject under treatment.

Accordingly, the present invention provides, in its broadest aspect, L-tryptophan for use in the treatment of obesity, especially in man, as an agent for the control of appetite when used in conjunction with a protein-restricted diet.

More specifically, in one aspect, the invention is for L-tryptophan when put up for use as an agent for the control of appetite as part of a protein-restricted dietary regimen, in particular, L-tryptophan in unit dosage form when put up for that use.

As used herein and in the claims the term "protein-restricted diet" or the like means a diet for any one particular individual which is reduced in its content of proteinaceous material to below that individual's normal average daily intake of said material. Typically, such a diet will generally comprise significantly less than about 250 grams per day, preferably 100 grams per day or less, of

proteinaceous material.

It is, of course, to be understood that the invention is concerned with the use of L-tryptophan in conjunction with a diet which while it is restricted in protein, and while it of necessity must be restricted in calories (if successful weight reduction is to be obtained), nevertheless is otherwise an essentially complete diet in a nutritional sense. That is to say the diet on a long term basis should be able to supply the patient's minimum nutritional requirements of minerals, vitamins, protein, carbohydrate and/or fat to maintain health.

In putting the invention into effect the L-tryptophan may be put up for use with either a solid carrier or a liquid carrier, provided it is a low-protein carrier. For example, the carrier may be an item of confectionary such as a chocolate, candy or "nutty" crunch bar, or say a chewing gum, or a carrier based on cereal or vegetable material such as a pasta, a crisp or chip. Also, a liquid carrier may be a beverage such as a beer or the like.

Preferably, in said one aspect of the invention, there is provided a composition for use in the treatment of obesity, which composition comprises L-tryptophan and a protein-restricted diet composition as carrier, the amount of L-tryptophan in the composition being such as to provide at least about 0.5 grams of L-tryptophan per daily amount of diet.

Again, the carrier may be either a solid diet carrier or a liquid diet carrier which provides a protein-restricted diet composition. More preferably, however, a composition for use in the treatment of obesity in accordance with the invention is a composition which comprises L-tryptophan and a protein-restricted formula diet as a carrier therefor, the amount of L-tryptophan in the composition being such as

to provide at least about 0.5 grams of L-tryptophan per daily amount of diet, and said diet comprising on a daily amount basis less than about 100 grams of proteinaceous material, and an energy level of no more than about 1000 Kcals.

Additionally, or alternatively, in said one aspect of the invention, there is provided a pack for use in the treatment of obesity, which pack comprises L-tryptophan put up for use as an agent for the control of appetite, together with instructions for using L-tryptophan in the treatment of obesity in conjunction with a protein-restricted diet. In such a pack the instructions typically may recommend the use of from about 0.5 to about 12 grams, preferably about 0.5 to about 10 grams per day of L-tryptophan in conjunction with a daily diet containing no more than about 100 grams per day of other proteinaceous material.

Furthermore, in another aspect, the invention provides a method for the treatment of obesity, especially in man, which method comprises giving to an overweight patient a daily diet in which the amount of proteinaceous material is restricted below the patient's normal average daily intake of protein, together with a daily dose of at least about 0.5 grams, typically from about 0.5 to about 12 grams, and preferably from about 0.5 to about 10 grams, of L-tryptophan as appetite suppressant.

It is, of course, to be understood that the daily dose of L-tryptophan can be administered in a plurality of amounts throughout the day. Thus, for example, where as described below the L-tryptophan is taken with a diet which itself is consumed three times a day, the daily dose of L-tryptophan may be divided into three one-third amounts each to be consumed with the diet at the three daily diet meals. Furthermore, the sub-division may be by any desired factor provided overall the necessary

daily dose is consumed.

As indicated above, it is preferred in carrying out the invention to employ an amount of proteinaceous material in the daily diet given to the patient which is restricted to a maximum of about 100 grams per day. Furthermore, the patient's daily diet should preferably also be restricted to a daily energy level of no more than about 1000 Kcals, in order to achieve a reasonably efficient rate of weight loss.

More preferably, the amount of proteinaceous material in the patient's daily diet should be at least about 15 grams per day, with an amount of proteinaceous material in the patient's daily diet of from about 15 to about 55 grams per day being especially preferred. Most preferably, however, the amount of proteinaceous material in the patient's daily diet should be from about 30 to about 45 grams per day.

In putting the invention into effect, the patient may be given a daily fresh food diet in which the amount of proteinaceous material is restricted. Preferably, however, the patient is given a daily formula diet in which the amount of proteinaceous material is restricted, both because the amount of proteinaceous material can thereby be controlled more accurately, and because the amounts of essential minerals and the amounts of vitamins given per day can be kept relatively independent of the daily energy level of the diet. Thus, the daily energy level can be kept below that at which with a fresh food diet the subject could not obtain all of the necessary minerals and/or vitamins in their recommended daily amounts.

More preferably, in the case where a formula diet is employed it may comprise a diet in accordance with that disclosed in British Specification No. 1,356,730 (as well as U.S. Specifications Nos. 4,009,265 and 4,298,601), the dislosures of each of which are

incorporated herein by way of reference. Such a formula diet is defined as one which comprises:

a) all the minerals required by man;

b) proteinaceous material consisting of:

i) a mixture of monomeric L-aminoacids, and/or

ii) natural proteins, and/or

iii) natural proteins reinforced with at least one monomeric L-aminoacid;

and

c) digestible carbohydrate;

such that the smallest amount of the dietary formulation containing at least the minimum daily requirements of each of the minerals required by man also contains:

A) at least about 15 grams of the proteinaceous material which must include at least the minimum daily requirements for man of all the essential L-aminoacids required by man; and

B) from about 15 to about 75 grams of the digestible carbohydrate

and such that the total calorific value of the said smallest amount of the dietary formulation is in the range of from about 160 Kcals to about 600 Kcals.

It is, of course, to be understood that in putting the present invention into effect within the context of the use of L-tryptophan together with such a formula diet, the various features of that earlier invention may be used as required or desired or preferred. Thus, preferably the diet will be one containing minerals (more preferably at least essentially all required minerals), vitamins (more preferably at least essentially all required vitamins) and a small amount of fat in accordance with the preferred aspects of the earlier disclosure.

While the necessary appetite-controlling effect of L-tryptophan can be obtained using daily amounts of the

compound of from about 0.5 grams and upwards, nevertheless the preferred upper limit per day is about 10 or 12 grams and, more preferably the patient should be given a daily dose of from about 3 to about 5 or 6 grams of L-tryptophan as appetite suppressant. Furthermore, the daily dose of L-tryptophan as given should be in addition to the patient's normal requirement of L-tryptophan as an essential aminoacid, which is usually about 0.25 grams in an adult male. Thus, in using L-tryptophan together with that commercially-available diet in accordance with British Specification No. 1,356,730 available inter alia in the U.K. and the U.S.A. under the trade mark "The Cambridge Diet", the L-tryptophan content of the formula diet can be ignored in calculating the necessary appetite-suppressant dosage of the active compound. Thus, a composition in accordance with the invention as defined above generally will contain an amount of L-tryptophan which reflects the above parameters and/or permits them to be followed in carrying out the method of the invention.

While, in accordance with the broadest aspects of the present invention L-tryptophan can be regarded as a powerful appetite suppressant per se within the context of any protein-restricted diet, it provides a significant and particularly useful advantage when used in conjunction with a very low calorie formula diet. With such a diet the first one to three days are always difficult, and similar difficulties can arise if the diet is broken at four weeks, as is often recommended. In some cases it may seem almost impossible to get back on such a diet after it is broken.

However, use of L-tryptophan solves those problems. In particular, L-tryptophan even permits the dieter to cheat (preferably only on special occasions) provided cheating is carried out on the basis of

consuming a treat which is low in protein. Since most overweight people like to cheat with treats which are low in protein, L-tryptophan is an ideal adjunct to the use of a very low calorie formula diet such as "The Cambridge Diet", with isolated bouts of cheating. Furthermore, the use of L-tryptophan introduces a degree of flexibility to dieting at about or below the 1000 kcal level, with protein restriction, which is hitherto unknown. By use of that compound the dieter in a very low calorie diet situation need no longer rely entirely on the mild ketosis effect to suppress hunger and need no longer fear the consequences of breaking the diet even for say one meal. Thus, the use of L-tryptophan can assist the dieter and the dietician in combining the use of very low calorie dieting regimens with other approaches to provide a variety and flexibility of approach which minimise the dieter's discomfort during the dieting period.

In putting the invention into effect it is essential on a daily basis to use at least about 0.5 grams of added L-tryptophan, along with a protein restricted diet, and preferably with a caloric restriction to about 1000 Kcals or below. However, a number of preferred features particularly enhance the effect of the L-tryptophan within that broad (but nevertheless new and surprising) context and further distinguish its use within that already new and surprising context, namely:

1. The use with or within the context of a very low calorie dietary regimen where the diet lowers blood sugar and encourages mild ketosis as with "The Cambridge Diet" and other diets within the disclosure of British Specification No. 1,356,370. Such diets are nutritionally complete, they are protein restricted and, furthermore, they are carbohydrate restricted to the extent that the

daily amount of carbohydrate given or supplied is a protein sparing amount of carbohydrate, generally from about 15 to about 75 grams per day. More preferably, as indicated in the specific Examples below, the amount of carbohydrate should be at least about 30 grams per day or more and up to about 70 grams per day. Thus, use of L-tryptophan in the present invention is preferably a use within the context of a diet which of itself lowers blood sugar and not within a context which deliberately causes insulin to be released by raising blood sugar.

2. The use of L-tryptophan at a preferred total level of over 3 grams per day, i.e. a preferred level at 3 grams plus the 0.25 gram or other amount supplied by the carrier, i.e. the diet <u>per se</u>.

3. The use of L-tryptophan over an extended period of time for the treatment of those who are significantly overweight. In particular, the use over a period of at least about 3 or 4 weeks, and typically much longer, where the appetite suppressant effect of the L-tryptophan becomes most useful.

In addition, the invention includes tryptophan for the manufacture of an agent for the control of appetite when used in conjunction with a protein-restricted diet.

The invention will now be described by way of example only with reference to the following Test Study and specific Examples.

Test Study

Twenty subjects in a test group were given tablets or capsules containing 500 mg of L-tryptophan. The subjects were not given any information about what they would be taking, although they were told that the tablets or capsules would help to reduce their hunger while they were reducing their weight on the basis of a very low calorie diet restricted in protein, and that if they consumed additional protein the treatment would not work. Dosage was given at 3 g per day and it was found that the administration of L-tryptophan at that level significantly reduced the compulsive desire to eat and, in particular, that it greatly alleviated the discomfort associated with the start-up phase of very low calorie dieting. In addition, it was found that where additional carbohydrate foods were taken, their consumption lead to rapid satiation and only modest amounts were consumed. However, consumption of protein-containing foods tended to negate the effect of the tryptophan and could increase hunger.

The very low calorie diet used in the study was "The Cambridge Diet", as sold by Cambridge Plan International in the U.S.A., and at least six of the subjects in the study were experienced with the use of the Diet and well motivated to use it to control weight. However, they had up until that time found it impossible successfully to re-start the Diet, but with the use of simultaneous administration of L-tryptophan each of the six subjects successfully resumed their dieting without any difficulty and sustained major new weight losses.

Example 1

A composition in accordance with the invention is formulated as follows:

Ingredients	Amount in grams per daily consumption of say three servings
Protein	34
Carbohydrate	44
Fat	3
L-tryptophan	3

The above composition on a daily basis provides a daily energy level of about 330 kcals.

Example 2

A composition in accordance with the invention is formulated as follows:

Ingredients	Amount in grams per daily consumption of say three servings
Protein	42
Carbohydrate	35
Fat	3
L-tryptophan	3

The above composition on a daily basis provides a daily energy level of about 330 kcals.

Example 3

A composition in accordance with the invention is formulated as follows:

Ingredients	Amount in grams per daily consumption of say three servings
Protein	70
Carbohydrate	30
Fat	2
L-tryptophan	3

The above composition on a daily basis provides a daily energy level of about 410 kcals.

Example 4

A composition in accordance with the invention is formulated as follows:

Ingredients	Amount in grams per daily consumption of say three servings
Protein	34
Carbohydrate	44
Fat	3
L-tryptophan	3
Vitamins and minerals	
Vitamin A	1.0 mg
Vitamin B_1	1.5 mg
Vitamin B_2	1.7 mg
Niacin	19.0 mg
Vitamin B_6	2.2 mg
Pantothenic Acid	7.0 mg
Biotin	200.0 mcg
Vitamins and minerals	
Folic Acid	400.0 mcg
Vitamin B_{12}	3.0 mcg
Vitamin C	60.0 mg
Vitamin D_3	10.0 mcg
Vitamin E	50.0 mg
Vitamin K	140.0 mcg
Calcium	800.0 mg
Phosphorus	800.0 mg
Magnesium	400.0 mg
Potassium	2.0 g
Sodium	1.5 g
Chloride	1.8 g
Iron	18.0 mg
Zinc	15.0 mg
Iodine	150.0 mcg
Copper	3.0 mg
Manganese	4.0 mg

Selenium	60.0 mcg
Molybdenum	150.0 mcg
Chromium	60.0 mcg

The above composition on a daily basis provides a daily energy level of about 330 kcals.

Example 5

A composition in accordance with the invention is formulated as follows

Ingredients	Amount per 1000g
Aminoacids	
L-Lysine HCl	10.02 g
L-Leucine	13.37 g
L-Isoleucine	8.45 g
L-Valine	9.31 g
L-Phenylalanine	9.63 g
L-Arginine HCl	16.40 g
L-Histidine HCl H_2O	4.10 g
L-Alanine	9.02 g
L-Aspartic Acid	19.19 g
L-Threonine	8.45 g
L-Proline	12.04 g
Glycine	14.69 g
L-Serine	6.19 g
L-Tyrosine ethyl ester HCl	10.54 g
L-Glutamine	31.69 g
L-Methionine	8.65 g
L-Tryptophan	32.60 g
Total	224.3 g

Ingredients	Amount per 1000g
Salts	
Potassium iodide	1.94 mg
Manganous acetate.$4H_2O$	237.0 mg
Cupric acetate.H_2O	32.35 mg
Sodium glycerophosphate	67.7 g
Sodium chloride	89.3 g
Ferrous ammonium sulphate	8.83 g

Zinc chloride	15.53 mg
Potassium hydroxide	13.35 g
Potassium chloride	53.1 g
Magnesium oxide	6.31 g
Sodium hydroxide	-
Calcium chloride.$2H_2O$	31.57 g
Total	270.6 g

Ingredients	Amount per 1000g
Vitamins	
Thiamin HCl	15.5 mg
Riboflavin	22.0 mg
Pyridoxin HCl	21.6 mg
Niacinamide	129.4 mg
Inositol	10.74 mg
d-Ca pantothenate	181.2 mg
Vitamin A acetate	64,700 Int. units
Vitamin D_2 - D_3	5,180 Int. units
d-Biotin	3.88 mg
Folic acid	21.6 mg
Ascorbic acid	1.035 g
Cyanocobalamin	0.194 mg
p-Amino benzoic acid	5.380 g
Choline bitartrate	2.990 g
Alpha-Tocopherol acetate	388.1 mg
Mendione (Vit. K)	776.4 mg
Total	11.0 g
Carbohydrate	
Glucose	54.3 g
Glucose-o-lactone	-
Dextrose oligosaccharides	418.0 g
Total	472.3 g
Fats	
Ethyl linoleate	25.9 g
Safflower Oil	-
Total	25.9 g

Emulsifier	
Polyoxyethylene sorbitan monooleate	25.9 g
Total	25.9 g

The above composition on a daily basis of consuming three servings amounting to a total of 100 grams per day provides a daily energy level of about 290 kcals.

Example 6

A pack in accordance with the invention comprises a seven-day supply of a Cambridge Diet product of Cambridge Nutrition Limited, having a formulation as set out in Example 4 above, except for the 3 grams of L-tryptophan, together with 42 tablets or capsules containing 500 mg of L-tryptophan. One portion of the Diet is taken three times a day as directed, e.g. at about 33 grams per serving, together with two 500 mg doses of L-tryptophan to provide a daily energy level of about 330 kcals, a daily amount of protein of about 34 grams and a daily amount of L-tryptophan of about 3 grams.

Example 7

Each of the above Examples is repeated except that the level of L-tryptophan is set at 5 grams per day.

Example 8

Each of the above Examples is repeated except that the level of L-tryptophan is set at 6 grams per day.

It is to be understood, of course, that the invention is not limited to the details of the above specific Examples or the above Test results. For example, the daily amount of protein can be above or below the exemplified amounts provided the protein is preferably within the range of from about 15 to about 100 grams per day. Also, the amount of L-tryptophan consumed per day preferably may be any amount within the range of from about 0.5 grams to about 10 or about 12

grams, and the daily energy level can be varied widely preferably within the range of from about 160 kcals up to about 1000 kcals.

CLAIMS

1. A composition for use in the treatment of obesity, which composition comprises L-tryptophan and a protein-restricted diet composition or other low-protein carrier, the amount of L-tryptophan in the composition being such as to provide at least about 0.5 grams of L-tryptophan per daily amount of diet.

2. A composition according to claim 1, wherein the amount of proteinaceous material on a daily basis is restricted to a maximum of about 100 grams per day of proteinaceous material.

3. A composition for use in the treatment of obesity, which composition comprises L-tryptophan and a protein-restricted formula diet as a carrier therefor, the amount of L-tryptophan in the composition being such as to provide at least about 0.5 grams of L-tryptophan per daily amount of diet, and said diet comprising on a daily amount basis less than about 100 grams of proteinaceous material and an energy level of no more than about 1000 Kcals.

4. A composition according to any one of the preceding claims, wherein the amount of proteinaceous material on a daily basis is at least about 15 grams per day.

5. A composition according to any one of the preceding claims, wherein the amount of proteinaceous material on a daily basis is from about 15 to about 55 grams per day.

6. A composition according to claim 5, wherein the amount of proteinaceous material on a daily basis is from about 30 to about 45 grams per day.

7. A composition according to any one of the preceding claims, wherein the formula diet carrier for the L-tryptophan comprises:

a) minerals required by man;

b) proteinaceous material consisting of:

i) a mixture of monomeric L-aminoacids, and/or

ii) natural proteins, and/or

iii) natural proteins reinforced with at least one monomeric L-aminoacid;

and

c) digestible carbohydrate;

such that the smallest amount of the dietary formulation containing at least the minimum daily requirements of said minerals required by man also contains:

A) at least about 15 grams of the proteinaceous material which must include at least the minimum daily requirements for man of all the essential L-aminoacids required by man; and

B) from about 15 to about 75 grams of the digestible carbohydrate

and such that the total calorific value of the said smallest amount of the dietary formulation is in the range of from about 160 Kcals to about 600 Kcals.

8. A composition according to any one of the preceding claims, wherein the amount of L-tryptophan on a daily basis is from about 0.5 to about 10 grams.

9. A composition according to claim 8, wherein the amount of L-tryptophan on a daily basis is from about 3 to about 5 grams.

10. A pack for use in the treatment of obesity, which pack comprises L-tryptophan put up for use as an agent for the control of appetite, together with instructions for using L-tryptophan in the treatment of obesity in conjunction with a protein-restricted diet.

11. A pack according to claim 10, wherein the instructions recommend the use of from about 0.5 to about 10 grams per day of L-tryptophan in conjunction with a daily diet containing no more than about 100 grams per day of other proteinaceous material.

12. The use of L-tryptophan for the manufacture of an

agent for the control of appetite when used in conjunction with a protein-restricted diet.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 86/00560

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[4]: A 61 K 31/405; A 23 L 1/305

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[4]	A 61 K; A 23 L

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X,Y	US, A, 4042687 (ARNOLD M. GANS, ALVIN J. GOREN, E.M. GORENBER) 16 August 1977 see claims 1-4; examples 1,2; column 6, lines 57-60; column 8, lines 59-61	1-12
X,Y	GB, A, 1289096 (MANUEL ALFRED XAVIER COCHEME et al.) 13 September 1972 see claims 1,4,5,9; page 1, lines 43-45; page 2, lines 94-116	1-12
X,Y	GB, A, 2129299 (ALEC JAMES COPPEN) 16 May 1984 see claims 1,3,5; page 1, lines 83-85, 90-97	1-12
X	EP, A, 0147699 (SOCIETE DES PRODUITS NESTLE S.A.) 10 July 1985 see claims 1-8; page 7, lines 24-27	1-12
X	US, A, 3809752 (WILLIAM H. FISHMAN et al.) 7 May 1974 see claim 1; example 2	1-12

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
19th November 1986	16 JAN 1987
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	M. VAN MOL

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON

INTERNATIONAL APPLICATION NO. PCT/GB 86/00560 (SA 14554)

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 12/12/86

The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US-A- 4042687	16/08/77	NL-A-	7613109	26/05/77
		BE-A-	848596	23/05/77
		FR-A,B	2332027	17/06/77
		US-A-	4025650	24/05/77
		DE-A-	2621000	02/06/77
		US-A-	4042688	16/08/77
		US-A-	4053589	11/10/77
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		AU-A-	1917976	11/05/78
		JP-A-	52096776	13/08/77
		SE-A-	7613087	25/05/77
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		DE-A-	1949774	27/05/70
		FR-A-	2019845	10/07/70
		BE-A-	739613	02/03/70
GB-A- 2129299	16/05/84	None		
EP-A- 0147699	10/07/85	CH-B-	658165	31/10/86
US-A- 3809752	07/05/74	None		